Notice of Allowability	Application No.	Applicant(s)	
	09/258,216	SODERLUND ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *4/27/2005*.

2. ☒ The allowed claim(s) is/are *82,85 and 88-101*.

3. ☒ The drawings filed on *26 February 1999* are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date ~~10/04;~~ 4/05
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☒ Other *10/04 1449 page 2 of 2 only* 90

Jehanne Sitton

JEHANNE SITTON
PRIMARY EXAMINER

6/20/05

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

The application has been amended as follows:

Please amend the TITLE to read as follows:

Method for Determining Specific Nucleotide Variations

REASONS FOR ALLOWANCE

2. The following is an examiner's statement of reasons for allowance:

Claim 82 is drawn to a method for detecting the presence or one or more specific nucleotides at a predetermined target position in a target nucleic acid by hybridizing a detection primer whose 3' terminus hybridizes to a nucleotide 3' ward (on the target) of the predetermined site such that no nucleotide of the same type as the one or more specific nucleotides to be detected be located in the target in any position between the position of the 3' terminus of the primer and the predetermined target position, and extending the primer in the presence of an admixture of a polymerization agent and a plurality of nucleoside triphosphates, the nucleoside triphosphates including at least one deoxynucleotide and at least one chain terminating nucleotide analogue, at least one deoxynucleotide defining a labeled deoxynucleotide comprising a detectable label or an attachment moiety capable of binding a detectable label, each

deoxynucleotide of the admixture of nucleoside triphosphates being complementary to a nucleotide which differs from any nucleotide to which a chain terminating nucleotide analogue of the admixture is complementary such that if a labeled deoxynucleotide is complementary to a specific nucleotide at the predetermined position, a detectable primer extension product is formed, and analyzing the extension reaction for the presence or absence of a detectable label in association with a labeled deoxynucleotide incorporated in an extension portion of the primer extension product to detect the presence of the corresponding specific nucleotide at the target position in the target nucleic acid. Claim 85 is drawn to a similar method wherein the nucleoside triphosphates include at least one deoxynucleotide and at least one chain terminating nucleotide analogue, at least one chain terminating nucleotide analogue defining a labeled chain terminating nucleotide analogue comprising a detectable label or an attachment moiety capable of binding a detectable label, each deoxynucleotide of the admixture of nucleoside triphosphates being complementary to a nucleotide which differs from any nucleotide to which a chain terminating nucleotide analogue of the admixture is complementary such that if a labeled chain terminating nucleotide analogue is complementary to a specific nucleotide at the predetermined position, a detectable primer extension product is formed of the detection primer extended to include an extension portion terminated with the labeled chain terminating nucleotide analogue, and analyzing the extension reaction for the presence or absence of a detectable label in association with a labeled chain terminating nucleotide analogue terminating an extension portion of the primer extension product to detect the presence of the corresponding specific nucleotide at the target position in the target nucleic acid. The claims require, among other embodiments, that the 3' terminus of the detection primer hybridize to the target at a position such that no nucleotide of

the same base as the one or more specific nucleotides to be detected be located on the target between the position that the 3' terminus of the detection primer hybridizes to and the predetermined target position; that extension is performed in the presence of an admixture of at least one deoxynucleotide triphosphate and at least one chain terminating nucleotide analogue; that either a deoxynucleotide triphosphate or a chain terminating nucleotide analogue of the admixture comprise a detectable label or comprise an attachment moiety which binds a detectable label; d) that the mixture of dNTP(s) and chain terminating nucleotide analogue(s) be such that the identity of the base of the dNTP(s) and the chain terminating nucleotide analogue(s) be different; and that detection of the presence of the specific nucleotide in the target is carried out by analysis of the primer extension product for the presence or absence of the labeled dNTP or labeled chain terminating nucleotide analogue incorporated by extension of the detection primer.

The closest prior art is as follows:

Holmes et al (WO 89/09282) discloses methods for sequencing DNA wherein the methods require the use of an admixture that consists of, for example, dCTP, dGTP, dTTP and ddATP. During the sequencing reaction, this admixture is added to a solution containing labeled dATP (pages 11-12). The claims are allowable over the prior art of Holmes because Holmes does not teach or suggest a method involving nucleotide triphosphates where each deoxynucleotide of an admixture of nucleoside triphosphates is complementary to a nucleotide which differs from any nucleotide to which a ddNTP of the admixture is complementary. The instant claims require that the identity of the base of the dNTP and the chain terminating

nucleotide analogue be different, whereas Holmes teaches using mixtures with all 4 dNTPs, and a ddNTP.

Skinner (Skinner et al; Nucleic Acids Research, vol. 14, p 6949-6964, 1985) teaches methods in which the misincorporation of nucleotides by AMV reverse transcriptase is studied. In one experiment (see page 6958), Skinner teaches primer extension reactions using a labeled primer together with an admix of unlabeled dGTP and ddATP. The claims are allowable over the prior art of Skinner because in the method of Skinner, no label is incorporated into the primer by the dNTP or ddNTP during primer extension as the nucleotides are unlabeled, nor does Skinner suggest or provide motivation for detection by analysis of a labeled dNTP or ddNTP incorporated by extension of the primer. The instantly pending claims are drawn to methods using a labeled dNTP or chain terminating nucleotide analogue and analysis of the extension reaction for the presence or absence of the labeled dNTP or chain terminating nucleotide analogue incorporated by extension of the detection primer.

Cohen (EP 0412883, published 2-13-91 and FR 2650840; cited in the IDS) disclose methods of sequencing a nucleic acid using an admixture of labeled ddATP, ddCTP, ddGTP and ddTTP. The claims are allowable over the prior art of Cohen because Cohen does not teach methods which require an admixture of both dNTPs and chain terminating nucleotide analogues (for example, ddNTPs) nor wherein each deoxynucleotide of an admixture of nucleoside triphosphates is complementary to a nucleotide which differs from any nucleotide to which a chain terminating nucleotide analogue of the admixture is complementary.

Mills (U.S. Patent No. 5,221,518) teaches methods for sequencing DNA wherein the methods require the use of the reagents of a primer, a polymerase and an admixture comprising

labeled A, T, C and G deoxynucleotides and A, T, C and G chain-terminating nucleotide analogues (see, e.g., columns 26, 36 and 54-55). The claims are allowable over the prior art of Mills because Mills does not teach or suggest using an admixture of dNTPs and ddNTPs such that a dNTP is complementary to a nucleotide which differs from any nucleotide to which a ddNTP of the admixture is complementary. The instant claims require that the identity of the base of the dNTP and the chain terminating nucleotide analogue in the mixture be different, whereas Mills is silent with regard to any specific mixture of dNTPs and ddNTPs. Mills only generally teaches that both dNTPs and ddNTPs can be used and references methods of sequencing DNA which require all 4 dNTPs and one ddNTP.

3. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jehanne Sitton

Jehanne Sitton
Primary Examiner
Art Unit 1634

6/20/05